REMARKS

Claims 9, 11-23 and 25-31 are currently pending in this application. Claim 9 has been amended to recite a method of treating an inflammatory component of cystic fibrosis with a tiotropium salt. The subject matter of claim 32 has been incorporated into claim 1 and thus, claim 32 has been cancelled.

Rejections under 35 U.S.C. §103

Claims 9, 11-15 and 31-32 remain rejected under 35 U.S.C. § 103(a) as being obvious over Gerd Cropp et al. ("Gerd" Am.J.Med. 1996) in view of Barnes (Chest 2000) and Boucher (US Pub. No. 2002/0099023). Further, claims 9, 11-14, 21-23 and 25-32 remain rejected under 35 U.S.C. § 103(a) as being obvious over Gerd in view of Barnes and Freund (WO98/27959, with US 2001/0008632 used as translation) and claims 9, 11-20 and 31-32 remain rejected under 35 U.S.C. § 103(a) as being obvious over Gerd in view of Barnes and Akehurst (U.S. Patent No. 6,919,069). Applicant respectfully traverses.

The case law and theory being relied upon by the Office pertains to a compound or composition claim, and not to the currently claimed method of treatment. However, the Office also cites new references, Disse (US Pub. No. 2002/0193394) and Hassan (U.S. Patent No) as supporting that tiotropium bromide was known to treat inflammation. This is in error because Disse is the publication of the parent of this application (10/096,810, filed 3/13/2002) and cannot be used as prior art against the present application. Hassan is also not prior art against the present application. Its International Filing is not an effective 102(e) date because the international filing was before Nov. 29, 2000. The 102(e) date is Aug. 8, 2001 (assuming fee, oath, and translation present at that date), which is after the present US provisional priority date of April 5, 2001. Additionally, the passage of Hassan cited by the Office does not relate to treatment of inflammation in a patient suffering from cystic fibrosis, which the present claims are now directed. Finally, if the Office were properly relying on these new references, it would be a

new ground of rejection which should not have been made Final.

In addressing the remaining rejections, applicant maintains the position that Gerd is a review article regarding the previous attempts of using bronchodilators "in the treatment of airway obstruction associated with cystic fibrosis;" see the introductory summary. Gerd makes clear to point out that the major cause of death from cystic fibrosis is respiratory failure which is secondary to airway obstruction. Thus, Gerd distinguishes "infected and abnormally tenacious secretions, airway inflammation and associated tissue edema, bronchospasm and secondary fibrosis" (emphasis added) from airway obstruction. Gerd discusses the use of a variety of types of bronchodilators by several means of administration, i.e., orally, intravenously and by inhalation of aerosolized forms. Gerd's review is that bronchodilators provide variable results for improved pulmonary function; see the Discussion and Summary. The only convincing results were for intravenous aminophylline and terbutaline. The results with aerosolized forms by inhalation was variable and relate specifically to treating airway obstruction.

As stated in the Office action, Gerd fails to provide any teachings regarding tiotropium salts. However, Gerd is further distinguished in that it also fails to teach a method for "treating an inflammatory component of cystic fibrosis" or a method "wherein the salt of tiotropium provides an anti-inflammatory activity," (emphases added). Gerd makes clear that the methods it reviews relate to treating airway obstruction in cystic fibrosis which Gerd itself specifically distinguishes from the inflammatory component of cystic fibrosis. Gerd ascribes no anti-inflammatory activity to the bronchodilation methods it reviews.

Further, Gerd provides a less than strong teaching regarding the use of inhaled bronchodilators for treating airway obstruction in cystic fibrosis. Contrary to its teachings regarding certain intravenously administered bronchodilators, Gerd makes clear that the intravenously administered compounds gave variable results. Thus, applicants dispute that Gerd leaves one of ordinary skill in the art with a reasonable expectation that the bronchodilators it discusses – let alone other ones – would be effective to treat airway obstruction in cystic fibrosis patients.

Barnes teaches that tiotropium bromide is a muscarinic antagonist used for the treatment of COPD. It is taught to provide a bronchodilating effect and thus is effective in opening airways to counter airway obstruction.

Boucher teaches a method for treating chronic obstructive airways diseases; see Abstract. Boucher includes cystic fibrosis, chronic bronchitis and ciliary dyskinesia among such diseases; see, e.g., page 1, para. 0004. Boucher's method involves administering a non-absorbable osmotically active compound to the patient, i.e., the "active compound;" see, e.g., page 1, para. 0007. Boucher also teaches that a bronchodilator can be administered together with this "active compound;" see, e.g., page 1, para. 0008.

Freund is directed to providing medicaments in the form of aqueous solutions to produce propellant-free aerosols.

Akehurst is directed to providing aerosol medicaments with a particular type of propellant and solvents.

Boucher, Freund and Akehurst were cited for their teachings regarding certain excipients in the compositions. Like the primary references, there is no allegation that these references teach that the bronchodilating compounds provide any other effect than a bronchodilating effect – i.e., treat airway dilation and obstruction.

None of the cited references provide any suggestion that a tiotropium salt would be useful for "treating an inflammatory component of cystic fibrosis" or a method "wherein the salt of tiotropium provides an anti-inflammatory activity," (emphases added). At most, the cited references suggest that tiotropium bromide would be useful as a bronchodilator for treating airway obstruction. Barnes provides such a teaching. However, Gerd itself makes clear that treating airway obstruction and treating inflammation are distinct effects. This is also made clear from the discussion in the specification at page 2, lines 13-30, of the instant specification. The teachings in the cited references that tiotropium salts are useful as bronchodilators for treating asthma or COPD are already stated as known in applicants' specification; see, e.g., pages 1 and 2. The discovery that the tiotropium salts provide an anti-inflammatory effect when administered

by inhalation in addition to their known bronchodilatory effect (see, e.g., page 2, lines 13-30, of the specification) is not taught or suggested by the cited references. Thus, the references fail to provide a reason for one of ordinary skill in the art to use a tiotropium salt for "treating an inflammatory component of a disease selected from cystic fibrosis" or a method "wherein the salt of tiotropium provides an anti-inflammatory activity."

For all of the above reasons, it is urged that the combined teachings of any of the cited references fail to render the claimed invention obvious to one of ordinary skill in the art. Thus, each of the three rejections under 35 U.S.C. §103 should be withdrawn.

It is submitted that the claims are in condition for allowance. However, the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

Respectfully submitted,

/Wendy Petka/

Wendy A. Petka, Reg. No. 53,459
Attorney for Applicant

BOEHRINGER INGELHEIM CORPORATION
Patent Department
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877
Telephone: (203) 791-6614
Facsimile: (203) 798-4408